

# National Institutes of Health Advisory Committee to the Director (ACD)

## Report of the ACD Working Group on High-Risk, High-Reward Research

June 2019

DRAFT

## Working Group Roster

### Members

- John Carpten, Keck School of Medicine of University of Southern California
- Molly Carnes, MD, University of Wisconsin
- Becky Miller, PhD, Office of Strategic Coordination/NIH
- Amy Palin, PhD, Eunice Kennedy Shriver National Institute of Child Health and Human Development/NIH
- Nicole Perry, Vanderbilt University
- Griffin Rodgers, MD, National Institute of Diabetes and Digestive and Kidney Diseases/NIH
- Scout, PhD, National LGBT Cancer Network
- Sandra Schmid, PhD, University of Texas Southwestern Medical Center
- Jason Sheltzer, PhD, Cold Spring Harbor Laboratory
- Hannah Valentine, MD, OD Scientific Workforce Diversity/NIH

### Co-Chairs

- Lawrence Tabak, DDS, PhD, OD/NIH
- Brendan Lee, MD, PhD, Baylor College of Medicine

## Acknowledgements

The co-chairs want to thank and acknowledgement to the working group members for their thorough participation and thoughtful discussions. Special thanks are extended to the leaders and staff from Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), Office of Strategic Coordination (OSC), who oversee the NIH High-Risk, High-Reward Research Initiatives and provided tremendous expertise and insight during the group's deliberations:

- James Anderson, MD, PhD; Director, DPCPSI
- Elizabeth (Betsy) Wilder, PhD; Director, OSC
- Ravi Basavappa, PhD; Program Leader, OSC
- Becky Miller, PhD; Program Officer, OSC

The group thanks the NIH program and review staff who provided information and details about the application and review processes for the HRHR Initiatives. The group also has an incredible amount of gratitude for the team in the Office of Portfolio Analysis in DPCPSI, who generated much of the data used to analyze each initiative in the HRHR research portfolio:

- George Santangelo, PhD; Director, Office of Portfolio Analysis
- Rebecca Meseroll, PhD; Science Writer and Analyst, Office of Portfolio Analysis

Data used in the analyses were also provided by the Division of Statistical Analysis and Reporting in the NIH Office of Extramural Research, and the working group would like to thank that team for their help.

In addition to those mentioned above, the working group sought input from other experts both external and internal to NIH. The co-chairs and members would like to thank these individuals for taking the time to brief them:

- Peter Highnam, PhD; Deputy Director, Defense Advanced Research Projects Agency (DARPA)
- Michael Lauer, MD; Deputy Director of Extramural Research, NIH
- Ted Zheng, MD, PhD, Program Director, NIAMS
- NIAMS RISK program team: Amanda Boyce, PhD; Hung Tsang, PhD; Tony Kirilusha, PhD

The working group would also like to thank Jessica Mazerik, PhD; Anna Mazzucco, PhD; and Becky Miller, PhD for their efforts in writing this report and preparing data and analyses to include.

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## Executive Summary

Over the last decade and more, NIH has developed high-risk, high-reward (HRHR) programs that are unique compared to NIH's more traditional funding programs. The HRHR programs encourage risk and creativity and ask applicants to put forth bold project ideas with limited or no preliminary data. The research funded under these initiatives has the potential to pay great dividends if successful, but due to the lack of preliminary data required, projects submitted under these initiatives are unlikely to fare well in traditional review. Riskiness and potential for driving innovative research in related areas are emphasized as part of the evaluation processes. These awards were initiated in the Common Fund but the concept and award activities have started to spread across NIH and some are now being implemented at several Institutes and Centers as well. This report is focused on the Common fund HRHR programs. The Common Fund now supports four such initiatives: the NIH Director's Pioneer Award, NIH Director's New Innovator Award, NIH Director's Transformative Research Award, and NIH Director's Early Independence Award. In spring 2018, the Advisory Council to the NIH Director assembled a working group of internal and external experts to evaluate the programs and assess the extent to which applications to these programs include women and other underrepresented groups, the diversity of scientific topics submitted and awarded under these programs, the institutional diversity, and the overall success of the programs. This group, the High-Risk, High-Reward working group, analyzed related data, gathered information, and deliberated for 18 months to reach recommendations for the ACD to consider adopting and transmitting to the NIH Director on the areas outlined above. In summary:

The working group agrees there is value in having HRHR programs and recommends that NIH expand them if possible.

The HRHR working group recognizes that encouraging women and underrepresented groups to serve as principal investigators on HRHR applications is of critical importance to increase their representation among the investigators and encourages specific outreach activities to alert these groups to these awards and diversify the applicant pool.

To increase racial, ethnic, and gender diversity of awardees, scientific diversity of topics, and range of institutions that receive awards, the group supports programmatic elevation of these factors by indicating they are of high priority in the funding announcements. The group also encourages NIH to enhance the racial, ethnic, and gender diversity of panels that review the HRHR awards.

The working group also highlighted the importance of safe, inclusive work environments for diversity in the scientific workforce overall, including in HRHR programs, and recommends that HRHR grantee organizations be required to provide assurances that they have effective, fair, and up-to-date policies to preserve a harassment-free environment; and to alert and work with NIH in the event they become aware of harassment findings related to HRHR grantees.

## Advisory Committee to the Director Working Group Report

### Introduction

#### Background

In the last 15 years, NIH has developed programs to fund research that has the potential to pay great dividends if successful, but is unlikely to fare well in traditional review due primarily to lack of preliminary data. These NIH high-risk, high-reward (HRHR) programs are unique compared to NIH's more traditional funding programs. They encourage risk and creativity and ask applicants to put forth bold project ideas with limited or no preliminary data. During evaluations, the project's riskiness and potential for driving innovative research in related areas are emphasized. These awards were initiated in the NIH Division of Program Coordination, Planning, and Strategic Initiatives, Office of Strategic Coordination, the Common Fund. These concept and award activities have started to spread across NIH and some are now being implemented at several Institutes and Centers as well. This report is focused on the Common fund HRHR programs. The Common Fund now supports four such initiatives: the NIH Director's Pioneer Award, NIH Director's New Innovator Award, NIH Director's Transformative Research Award, and NIH Director's Early Independence Award (Table 1).

#### NIH Director's Pioneer Award (DP1)

The NIH Director's Pioneer Award was initiated in 2004. These awards support highly innovative researchers at any career stage who propose bold research projects with the potential to have an unusually broad scientific impact. To be considered "pioneering," the proposed research must reflect ideas that are substantially different from those being pursued in the investigator's research program or elsewhere. No detailed experimental plan or detailed budget is expected. The major component of the application is a five-page essay in which the investigator describes the project, its innovation and significance, the investigator's history of being highly innovative, and why the proposed project is suitable for the NIH Director's Pioneer Award. Three letters of reference must be provided.

#### NIH Director's New Innovator Award (DP2)

Initiated in 2007, the NIH Director's New Innovator Award supports highly innovative research from promising Early Career Stage Investigators (defined as those within ten years of completion of their terminal research degree or clinical training and who have not yet received substantial NIH support). No detailed experimental plan or preliminary data are required. Rather, the major component of the application is a ten-page essay in which the Principal Investigator describes (1) the significance of the problem/challenge being addressed; (2) the general approach to be taken to address the problem/challenge; (3) why the project is unusually innovative; and (4) the qualities and experiences of the Principle Investigator that make him/her especially well-suited to pursue such research.

#### NIH Director's Transformative Research Award (R01)

In 2009, the NIH Director's Transformative Research Award was started. This initiative supports exceptionally innovative and/or unconventional research projects that have the potential to

create or overturn fundamental paradigms. Multiple Principal Investigators and large budget applications are welcome. Though the application uses the standard R01 application, the requested information is very different from the standard R01. No detailed experimental plan or preliminary data are required. Rather, in the “research strategy” component, the investigators are asked to describe the challenge or problem being addressed, why it is important, and why the proposed approaches to addressing this major challenge or problem are unusually innovative. In addition, the investigators are asked to use the “specific aims” component to distill their proposal into a one-page summary in which they explicitly address the challenge, innovation, and impact of what they propose and the rationale of their approach.

#### NIH Director’s Early Independence Award (DP5)

The NIH Director’s Early Independence Award started in 2010. This award accelerates the entry of exceptional junior investigators (within approximately one year of terminal research degree or completion of residency) into positions of independent research by omitting the traditional post-doctoral training period. The NIH Director’s Early Independence Award review places a strong emphasis on the qualities of the investigator and the environment provided by the host institution. Because the host institution must provide the junior investigator with substantial support (an independent research position and the necessary resources and mentorship to successfully establish an independent research program), institutions are limited to two applications per funding opportunity and are responsible for the selection of candidates.

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	Pioneer Award	New Innovator Award	Transformative Research Award	Early Independence Award
<b>Target Group</b>	Individuals of exceptional creativity proposing pioneering approaches	Individual early stage investigators of exceptional creativity proposing research with uncommonly high impact potential	Individuals or teams proposing transformative research that may require very large budgets	Outstanding junior scientists wishing to “skip the postdoc” and immediately begin independent research
<b>Eligibility</b>	Open to all career stages	<ul style="list-style-type: none"> <li>• Receipt of most recent doctoral degree (e.g., Ph.D., M.D., D.D.S., D.V.M., Pharm.D., or equivalent) or end of postgraduate clinical training within the past 10 years of application submission date</li> <li>• Must be “new investigator” (never been awarded an R01 or equivalent NIH grant)</li> </ul>	Open to all career stages	<ul style="list-style-type: none"> <li>• Must receive terminal research degree or complete postgraduate clinical training within previous 15 months or expect to do so within following 12 months of application submission date</li> <li>• Maximum of two applications per institution (or grant-submitting entity)</li> <li>• Candidate must be in non-independent research position at time of application</li> </ul>
<b>Preliminary Data</b>	Not required; may be included	Not required; may be included	Not required; may be included	Not required; may be included
<b>Research Strategy</b>	5-page limit; respond to questions about the challenge, potential impact, suitability for the award, investigator’s innovativeness, and how the research qualifies as new research direction	10-page limit; respond to questions about significance and potential impact, innovativeness of approach, how risks and challenges will be addressed, suitability for the award, and investigator’s qualifications	12-page limit; respond to questions about the challenge, innovativeness of approach, potential impact, and appropriateness for the award	12-page limit; respond to questions about the challenge, innovativeness of approach, investigator’s qualifications, and plans for development; in addition, host institution must provide details of commitment
<b>Reference Letters</b>	3 letters required	None accepted	None accepted	3-5 letters required
<b>Effort</b>	Major portion (at least 51%) of research effort must be devoted to activities supported by the award	Minimum of 25% of research effort must be devoted to activities supported by the award	Effort should be commensurate with project needs and follow general guidelines for other NIH projects of similar size, complexity, and duration	9.6-person months (80% effort) must be devoted to award project for first 2 years, followed by 9.6-person months towards independent research in general
<b>Budget</b>	<ul style="list-style-type: none"> <li>• No detailed budget information submitted</li> <li>• Awards of \$700,000 per year for 5 years, plus standard F&amp;A (indirect) costs</li> </ul>	<ul style="list-style-type: none"> <li>• No detailed budget information submitted</li> <li>• Awards of \$1.5 million disbursed in the first year of the 5-year project period, plus standard F&amp;A (indirect) costs</li> </ul>	<ul style="list-style-type: none"> <li>• No limit on budget up to maximum funds available for the entire initiative</li> <li>• No prior approval required for budgets over \$500,000 in direct costs in any year</li> <li>• 5-year project period</li> </ul>	Awards up to \$250,000 per year for 5 years, plus standard F&A (indirect) costs
<b>Multiple PIs</b>	Only one PD/PI may be designated on the application	Only one PD/PI may be designated on the application	More than one PD/PI allowed	Only one PD/PI may be designated on the application
<b>Review Format</b>	Multi-phased, “editorial board,” interview of finalists	Multi-phased, “editorial board”	Multi-phased, “editorial board”	Multi-phased, “editorial board”

Table 1 Comparison of the four HRHR initiatives.

## Review Processes

The NIH peer review process for each initiative is organized and overseen by the NIH Center for Scientific Review with a moderately different review process for each one. For each award, finalists (or submitters of “discussed applications in the case of the Transformative Research Award) are given the opportunity to respond to their summary statements in a two-page letter. These letters are reviewed by members of the High-Risk, High-Reward Research program working group, composed of NIH staff from various NIH institutes and centers. While most of the awards are made with significant consideration given to priority score, the working group

members review the application, summary statement, and summary statement response to recommend additional funding decisions based on programmatic priorities. The individual ICs also have the opportunity to fund applications of their choice. The second-level review is conducted by the Council of Councils, which votes *en bloc* to approve the reviews.

#### *Pioneer Award Review Process*

The initial level of peer review is conducted by a scientific review group in a special emphasis panel convened each year for the review of Pioneer Award applications. The review focuses on the investigator's creativity, innovativeness of the research approaches, and the project's potential impact on an important biomedical or behavioral research problem.

The review occurs in two phases. Phase I is conducted by "mail reviewers." Two of the three mail reviewers for each application have expertise in the broad area of the application while the third has expertise outside the area. In phase II, a separate panel consisting of scientific leaders known for their broad scientific perspective uses information from the Phase I reviews to select the 25 or so most meritorious applicants (termed finalists). These finalists are invited for an in-person interview in Bethesda with the phase II panel. The panelists provide individual scores for each finalist; these are used to calculate the overall priority score. In addition, the panel assigns each of the finalists by consensus to one of three bins (high, medium, and low) to reflect the overall enthusiasm of the panel.

Finalists receive a summary statement, or summary of the panel's critiques and level of enthusiasm. Non-finalist applications are considered "Not Discussed," and summary statements contain the critiques of the mail reviewers.

#### *New Innovator Review Process*

The initial level of peer review is conducted by a scientific review group in a special emphasis panel convened each year and emphasizes the investigator's creativity, the innovativeness of the research approaches, and the potential of the project, if successful, to have a significant impact on an important biomedical or behavioral research problem.

The review proceeds in two phases. In phase I, "mail reviewers," who are eminent scientists matched relatively closely to the topic of the application, provide independent comments and scores. Phase II is conducted by a panel of scientific leaders known for their broad scientific perspective. Informed by the phase I reviews, the panel selects a subset of applications to discuss and score at an in-person meeting.

Summary statements of those applications selected for phase II contain a summary of discussion and the critiques from the three assigned phase II panel members. All other applications are considered "not discussed;" summary statements for these applications contain the critiques from the phase I mail reviewers.

#### *Transformative Research Award Review Process*

The initial level of peer review is conducted by a scientific review group in a special emphasis panel convened each year and emphasizes significance, innovation, and transformative potential of the proposal. The review occurs in three phases. In phase I, the "editorial board," consisting of eminent, broad-thinking scientists, assesses all the applications received and

identifies a subset that they deem to have the most transformative potential. In phase II, this subset of applications is evaluated by “mail reviewers” who have scientific and technical expertise in the topic of the application. The critiques from the mail reviewers are then conveyed to the editorial board. In phase III, informed by the mail reviewer critiques, the editorial board identifies a further subset to discuss and score in an in-person panel meeting. All other applications are considered “not discussed” and are not scored. Summary statements of discussed applications contain the editorial board’s summary of discussion and the critiques of the mail reviewers. The summary statements of applications advancing to the mail review stage (phase II) contain mail reviewer critiques. The summary statements of applications not advancing to the mail review stage contain a summary of the review process used for Transformative Research Award applications but contain no evaluative comments.

#### *Early Independence Award Review Process*

The initial level of peer review is conducted by a scientific review group in a special emphasis panel convened each year. The review emphasizes the investigator’s creativity, the innovativeness of the research approaches, and the potential of the project, if successful, to have a significant impact on an important biomedical or behavioral research problem. The review occurs in two phases. Phase I is conducted by “mail reviewers.” The mail reviewer assignment is based on close matching of reviewer expertise to the topic of the application. Mail reviewers provide scores and comments based on the review criteria published in the Funding Opportunity Announcement. In phase II, informed by the phase I reviews, a separate panel, consisting of scientific leaders known for their broad scientific perspective, selects a subset of applications to consider further. The panel discusses and scores these applications in an in-person meeting. In previous (FY2011-FY2018) competitions, finalists were selected for an in-person interview with phase II panelists. Interviews were eliminated for the FY2019 competition in response to concerns about potential bias against women during the interview stage. Summary statements of finalist applications summarize the panel’s enthusiasm and the critiques of the mail reviewers. Non-finalist applications are considered “not discussed,” and summary statements contain the critiques of the mail reviewers but no comments from the panel.

#### *Process for Deliberations*

The ACD Working Group on High-Risk, High-Reward Research conducted multiple meetings both face-to-face and via teleconference between its convening in April 2018 and its final draft report to the Advisory Committee to the Director in June 2019.

As part of their evaluation process, they reviewed professional, independent outcome analyses of select years of the Pioneer and New Innovator Awards. The Office of Portfolio Analysis (OPA) within DPCPSI, Office of the Director, provided internal data analyses from NIH grants and other databases, and the Office of Strategic Coordination provided additional information and expertise to describe how prospective and funded investigators of NIH HRHR programs compared to their peers using several different metrics, such as success rates in subsequent NIH grant applications, and impact of their scientific work.

As per the charge, the working group reviewed the NIH HRHR programs as detailed below.

Of note, the [ACD Next Generation Research Initiative](#) working group also examined the HRHR awards as part of their deliberation process. That group made the formal recommendation to the ACD to expand pathways for funding Early Stage Investigators (ESIs) through programs that do not require preliminary data.<sup>1</sup> The group cited the New Innovator program as an example. Although the Next Generation Research Initiative working group did not support the idea of increasing the New Innovator program, since not all ESI research would be considered high-risk, high-reward, they applauded having a pathway for this unique type of research.

The Next Generation Working Group also recommended that NIH require broad and recurrent evidence-based training on unconscious bias for program staff, scientific review officers, and peer reviewers.<sup>1</sup> This recommendation is in line with the findings of the HRHR working group.

### Summary of Observations

#### Review the effectiveness of distinct NIH HRHR research programs that emphasize exceptional innovation

Before the ACD HRHR working group existed, the Common Fund commissioned independent evaluations for a subset of cohorts from its two oldest programs, the Pioneer Award and the New Innovator. These programs were selected for review because for outcome evaluations, the initiatives needed to be ongoing for long enough to allow its grantees to produce results. Evaluations were conducted by professional contractors and took approximately one year to complete. The analyses and results are summarized.

#### NIH Director's Pioneer Award Evaluation

In 2012, the independent entity Science and Technology Policy Institute of the Institute for Defense Analysis completed an evaluation of the NIH Director's Pioneer Award.<sup>2</sup> The evaluation addressed two primary questions:

1. To what extent does the research supported by the Pioneer Award produce unusually high impact?
2. To what extent are the research approaches used by Pioneer awardees highly innovative?

The scientific impact and innovation of Pioneer research from FY2004-2006 cohorts were assessed through bibliometrics and expert analysis of publications using two main comparison groups: matched R01 grants (i.e., topics, costs) and Howard Hughes Medical Institute (HHMI) investigators. In general, the evaluation found Pioneer Award research is more impactful and

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<sup>1</sup> [https://acd.od.nih.gov/documents/presentations/12132018NextGen\\_report.pdf](https://acd.od.nih.gov/documents/presentations/12132018NextGen_report.pdf)

<sup>2</sup> <https://commonfund.nih.gov/sites/default/files/HRHR%20PA%20FY%202004-2006%20Outcome%20Evaluation.pdf>

innovative than that conducted by matched R01 investigators and about as impactful and innovative as HHMI investigators.

#### NIH Director's New Innovator Award Evaluation

In 2016, the independent entity Science and Technology Policy Institute of the Institute for Defense Analysis completed an evaluation of the NIH Director's New Innovator Award<sup>3</sup>. The evaluation addressed two primary questions:

1. Is New Innovator research significantly more innovative, high risk, or impactful than traditionally funded NIH research?
2. What are the impacts, both positive and negative, of New Innovator awards on the careers of awardees compared to the career impacts of a comparable traditional NIH award?

New Innovator Award cohorts from FY2007-2009 were compared to matched early career stage R01 investigators (i.e., degree type, area of research, publication frequency prior to award, gender, institution type) and New Innovator Award finalists who were not selected for funding. Bibliometric analyses were used to assess impact and productivity and expert reviews of publications for impact and innovativeness. The evaluation found New Innovator research is more innovative, risky, and impactful than similarly staged R01 investigators, and that the New Innovator Award does not positively or negatively impact the careers of awardees compared to the impact of an R01 on its recipients. For example, they had similar success in securing additional funding compared to R01 investigators and were similarly successful in advancing their careers. However, the New Innovator awardees' projects did get featured more in the press, and on journal covers.

In summary, the Pioneer and New Innovator Awards programs were evaluated using various metrics and closely-matched controls, and show greater impact and trend toward higher productivity over traditional R01 grants. NIH should build upon the successes of these programs, while at the same time, ensuring that the prospective and funded investigators reflect the diversity of biomedical researchers and the U.S. population, while at same time ensuring that applicants and awardees reflect the diversity of biomedical researchers and the U.S. population.

#### Assessing the productivity of HRHR Awards

The OPA performed several analyses to assess the productivity of the HRHR awards. This approach was used in addition to the independent, year-long evaluations that were performed for several years of the Pioneer and New Innovator awards. OPA analyzed the influence of the four HRHR programs based on the Relative Citation Ratio (RCR) and other metrics. RCR is a

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[https://commonfund.nih.gov/sites/default/files/HRHR%20New%20Innovator%20Award%20Outcomes%20Evaluation%202007-2009\\_508%20compliant.pdf](https://commonfund.nih.gov/sites/default/files/HRHR%20New%20Innovator%20Award%20Outcomes%20Evaluation%202007-2009_508%20compliant.pdf)

time- and field-normalized measure of influence; the RCR of a typical (median) NIH-funded publication is 1.0.<sup>4</sup> The analysis included awards that began in FY 2011 and excluded those in FY 2017 and FY 2018, comparing the productivity of HRHR awards with NIH R01 awards. During its deliberations, the working group had several discussions about what group(s) served as the most appropriate comparator for the HRHR awards, but after considering several options, deciding to use the full NIH R01 pool. Similar productivity analyses were also performed using multivariate regression to consider a broad range of potential confounding factors, and the results were consistent with the data and conclusions included in this report. Productivity of awards was assessed by measuring publication statistics for each award type, for example, the number of publications and the percentage of awards producing at least one publication (Table 2). Influence of publications was assessed using RCR, which included both primary literature and reviews. A high RCR indicates at least one publication with an RCR  $\geq 3.0$ , which is approximately the 85<sup>th</sup> percentile (Figure 1). The highest citation activity indicates publications that are changing the field.

Award Type	Number of awards	Number of pubs	Pubs per award	Awards with $\geq 1$ pub	Awards with $\geq 1$ high RCR pub <sup>†</sup>
Transformative	76	1140	15.00	68 (89.5%)	51 (67.1%*)
Pioneer	70	837	11.96	64 (91.4%)	38 (54.3%)
Independence	88	656	7.45	75 (85.2%)	41 (46.6%)
Innovator	280	2383	8.51	252 (90.0%)	120 (42.9%)
NIH R01s	22,559	208,129	9.23	20,375 (90.3%)	8883 (39.4%)

Table 2, numbers of awards and associated publications

\* Statistically significant difference relative to NIH R01s  $p < 0.01$

<sup>†</sup> RCR  $\geq 3.0$  (~85<sup>th</sup> percentile)

<sup>4</sup> B. Ian Hutchins, Xin Yuan, James M. Anderson, and George M. Santangelo. Relative Citation Ratio (RCR): A New Metric That Uses Citation Rates to Measure Influence at the Article Level. (September 2016) PLoS Biol. 14(9): e1002541.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5012559/>

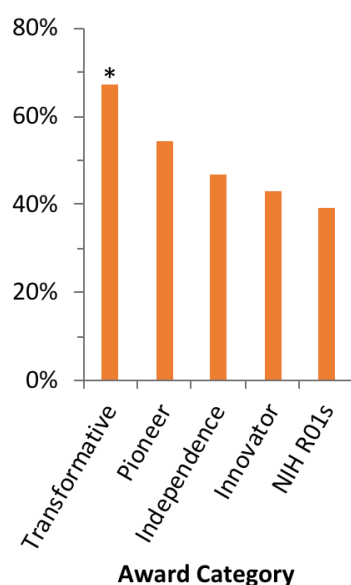


Figure 1, Percent of HRHR awards with high RCR values ( $\geq 3.0$ )

\* Statistically significant difference relative to NIH R01s  $p < 0.01$

Overall, in studying these data, the working group concluded that the HRHR awards funded highly productive research compared to the work funded under traditional NIH R01s. Specifically, HRHR publications were more influential, with higher mean and median RCR, higher mean and median weighted RCR (wRCR, or the sum of all RCRs for a given category<sup>5</sup>) per award, and a higher percentage of awards with at least one publication at or above the 85<sup>th</sup> percentile for RCR (Table 3).

Award Type	Pubs per Award	Mean RCR	Median RCR	wRCR	Mean wRCR per award	Median wRCR per award
Transformative	15.00	4.16*	1.96*	3512	58.53*	27.41*
Pioneer	11.96	4.77*	1.70*	2874	55.27	13.56
Independence	7.45	3.83*	1.90*	1705	28.41	9.21

<sup>5</sup> <https://icite.od.nih.gov/help>

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Innovator	8.51	2.67*	1.29*	4372	20.43	10.77
NIH R01s	9.23	2.20	1.19	326,103	18.57	8.01

Table 3, Type 1 HRHR and NIH R01 awards, FY2011-FY2016

\* Statistically significant difference relative to NIH R01s  $p < 0.01$

### Clinical and Technological Impact of HRHR Awards

Using methods developed internally, the Office of Portfolio Analysis compared the percentages of HRHR awards with clinical or technological impact with the percentages of traditional R01 awards. Awards resulting in one or more clinical trials or guidelines or at least one publication cited by a clinical trial or guideline with results counted as having clinical impact. Awards that resulted in one or more patents or at least one publication cited by a patent were counted as having technological impact.

Award Type	Number of awards	Awards with clinical impact	Awards with technological impact
Transformative	76	25 (32.9%)	35 (46.1%*)
Pioneer	70	17 (24.3%)	20 (28.6%*)
Independence	88	25 (28.4%)	15 (17.0%)
Innovator	280	58 (20.7%*)	58 (20.7%)
NIH R01s	22,559	7708 (34.2%)	3617 (16.0%)

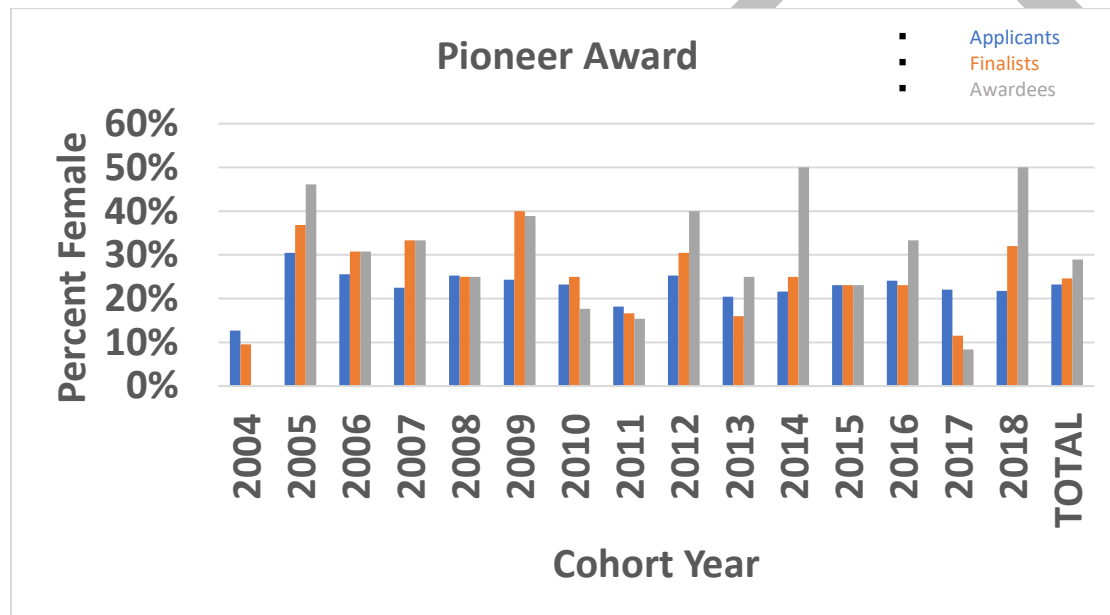
Table 4, Type 1 HRHR and NIH R01 awards, FY2011-FY2016; \* Statistically significant difference relative to NIH R01s  $p < 0.01$

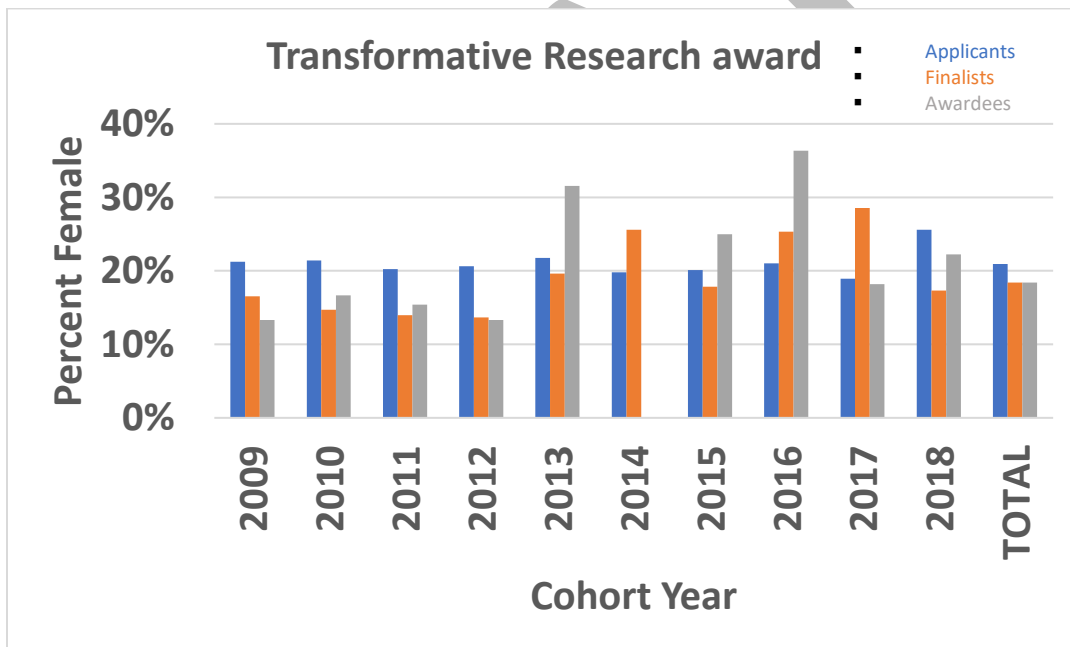
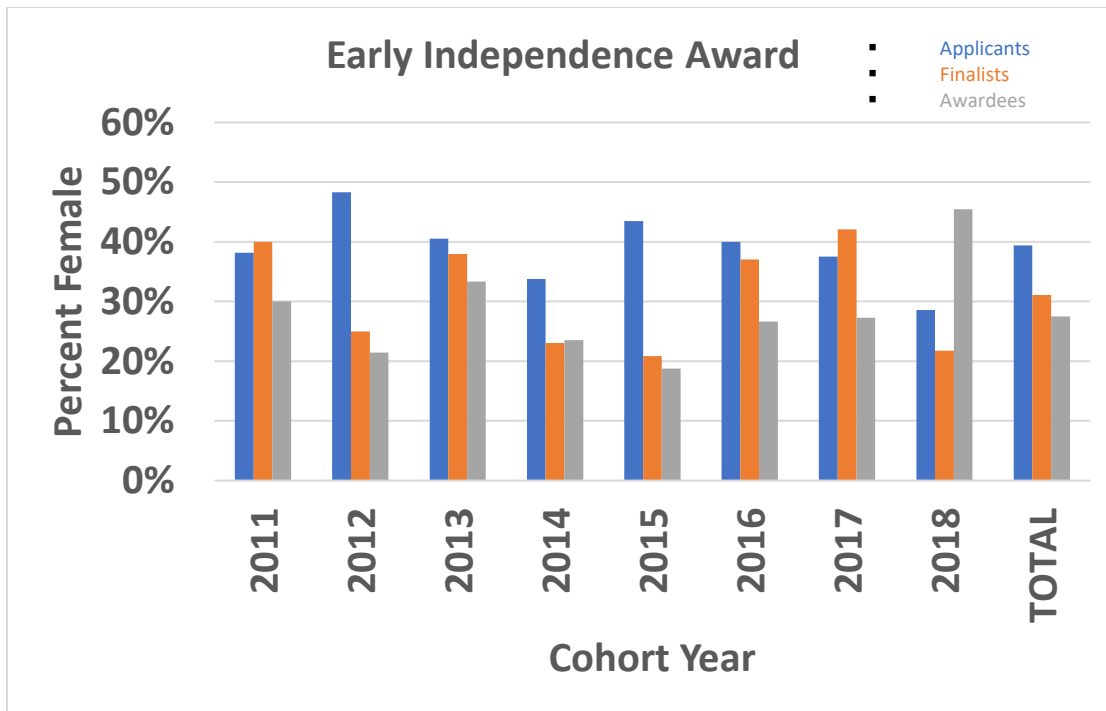
As compared to NIH R01s, a higher percentage of HRHR awards have technological impact, while a lower percentage of HRHR awards have had clinical impact (Table 4). This result can be explained by the inherent properties of the HRHR awards. One of the goals of the HRHR program is to fund ideas that will have broad impact across biomedical research; and technology development projects tend to be broader-reaching and accessible to multiple fields,

potentially giving an advantage to applicants proposing, and ultimately projects developing new technologies.

#### Analysis of the participation of women and underrepresented groups and in the applicant and awardee pools to identify possible causes for their underrepresentation

Across all years of awards, and for all applicants, finalists and awardees, the working group evaluated participants at each stage based on gender. Importantly, these data are collected not through grant applications, but through the applicant's eRA account, so reviewers do not have access to this information during the review process. Furthermore, for this evaluation, to ensure the privacy of grant applicants, ethnicity and URM data were provided to the working group in aggregate. The group concluded that the aggregate numbers and were too small to provide meaningful analyses, and strongly concurred that efforts are needed to encourage these groups to apply to these HRHR awards.





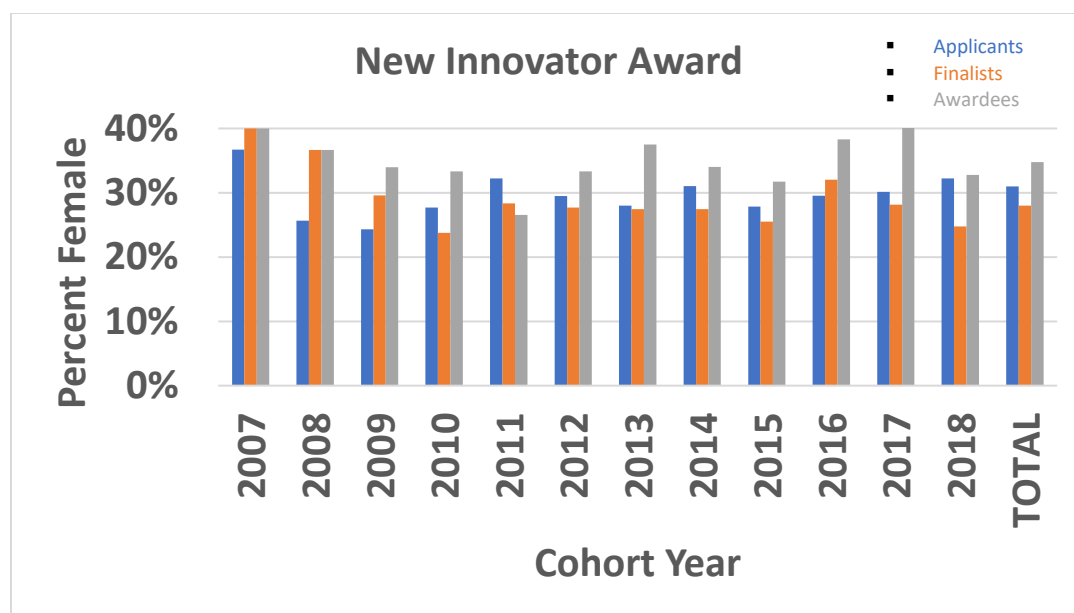


Figure 2, Percentages of female investigators of institution applicants, finalists, and awardees for each year of each type of award.

For each award, the group explored the percentage of females (Figure 2 and Table 5).

Female Participation			
	% Female Applicants	% Female Finalists	% Female Awardees
Pioneer	23%	25%	29%
<b>New Innovator</b>	<b>31%</b>	<b>28%</b>	<b>35%</b>
Transformative Research	21%	18%	18%
<b>Early Independence</b>	<b>39%</b>	<b>31%</b>	<b>27%</b>

Table 5, Trends in gender representation for lifetime of each award, through 2018. Values displayed are percentage of female applicants, awardees, or finalists for each HRHR award. Highlights indicate statistical significance.

For each of the three categories, a two-tailed paired t-test ( $p$  value  $\leq 0.05$ ) was used to interrogate the mean difference between

- Percentage of applicants and awardees
- Percentage of applicants and finalists
- Percentage of finalists and awardees

For gender, the percentage of New Innovator Award female investigators of institution awardees increased compared to both percentage of applicants and finalists ( $p = 0.003$ ). For the Early Independence Award, percentage of female investigators of institution awardees

decreased compared to the percentage of applicants ( $p = 0.036$ ). The working group observed that self-nomination among women for HRHR awards is low, especially when compared to the percentage of women investigators of institution applicants R01s.

The working group also discussed other underrepresented groups, including underrepresented minorities (URM, defined here includes individuals who identify as African American or Black, American Indian or Alaska Native, Hawaiian or Other Pacific Islander<sup>6</sup>), and ethnicity (Hispanic or non-Hispanic). For this evaluation, to ensure the privacy of individuals identified in grant applications, ethnicity and URM data across all HRHR were averaged and provided to the working group in aggregate. The group concluded that the aggregate numbers were too small to provide meaningful analyses, and strongly concurred that efforts are needed to encourage these groups to apply to these HRHR awards.

#### Examination of diversity of scientific topics and institutional diversity in the applicant and awardee pools

The Office of Portfolio Analysis used a computational approach, Word2vec<sup>7</sup><sub>OPA</sub>, to characterize the content of the HRHR applications and awards by clustering applications and awards based on word similarity. This allowed for visualization and comparisons among the four types of awards. Taken together, HRHR applications and awards mapped to a narrow range of topics that varied widely in award rates (Figure 3). HRHR awards mapped to a relatively small subset of topics in the biomedical research landscape. Specifically, 14.2% of the topics accounted for more than half of the HRHR applications, while 10.1% of the topics accounted for more than half of the HRHR awards.

When examining scientific topic areas, examples of underrepresented topics include population studies, epidemiology, and studies looking at health outcomes. Clinical topics are also not well represented, and this distribution may explain the lower percentage of HRHR awards that have had clinical impact relative to R01s.

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<sup>6</sup> Asian Americans were not included as an underrepresented group for these deliberations by the group due to their participation and representation being equivalent to Caucasian individuals.

<sup>7</sup> Tomas Mikolov, Kai Chen, Greg Corrado, Jeffrey Dean. Efficient Estimation of Word Representations in Vector Space. (September 2013) *arXiv:1301.3781v3*.  
<https://arxiv.org/abs/1301.3781>

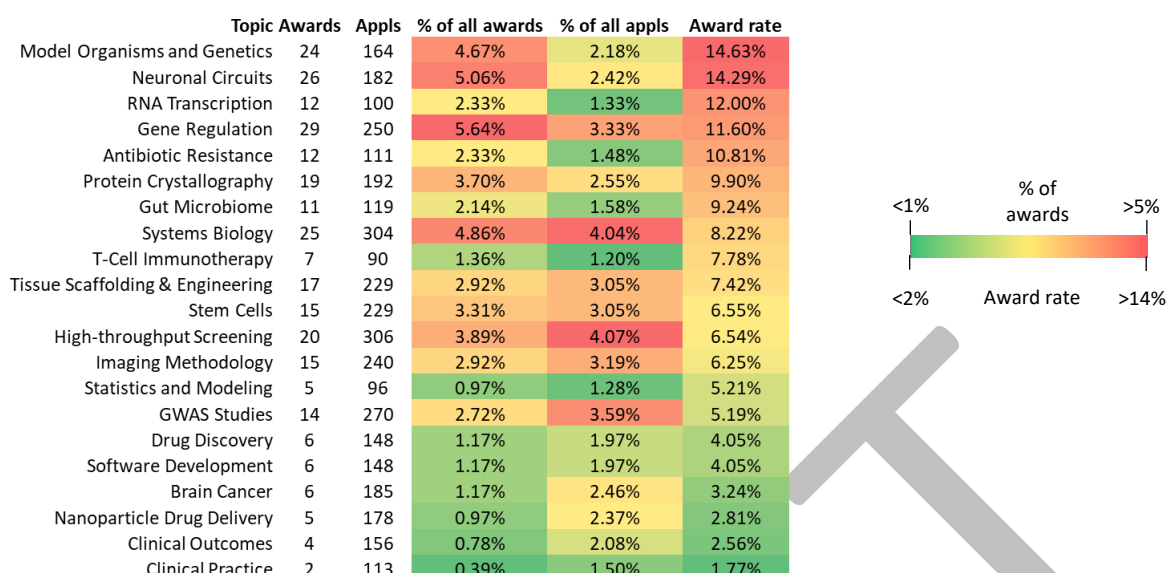


Figure 3, Percentages of HRHR applications and awards that represent specific scientific topics. The 21 topics (14.2% of all topics) that comprise over half of all HRHR applications are shown. Red indicates higher values, while green indicates lower values.

Another factor that may introduce bias and contribute to the observed distribution of topics is that other than the Transformative Research Award, these awards tend to entail topics that are inherently less feasible by a single investigator; they are team science projects that may not fare well under HRHR programs as they are currently designed and reviewed. Possible ideas to address this included having team-based HRHR awards, or building into the applications the option to link to or describe a team (rather than just support letters for the primary investigators). These and other solutions are discussed further in the recommendations section.

The working group examined the organizations and institutions of prospective and funded investigators within HRHR programs. The Office of Portfolio Analysis analyzed the level of NIH investment for all 116 organizations that had at least one HRHR award between FY2011-FY2016 based on annualized R01 dollars per applicant in the preceding five years (FY2006-FY2010). The award rates were sorted by dollars/applicant and color-coded to visualize the spectrum of success from most successful (red) to least successful (green; Figure 4). Organizations with the highest funding levels had the highest percentage of awards and the highest award rates.

The working group was concerned that lower-resourced institutions and organizations were not as well-represented among HRHR awards as higher-resourced institutions. They also agreed that incorporating geographic diversity and having lower-resourced institutions and organizations better represented would strengthen the overall HRHR programs. To enhance institutional diversity, the working group members deliberated about three options:

- To include institutional diversity in HRHR funding announcements, thereby elevating it as a program priority;
- To cap the number of applications each institution can submit; or

- To cap the number of applications each institution can submit, but factor in size of institutions and scale the permissible number of submissions accordingly.

As of the writing of this report, an institutional cap applies only to the Early Independence Award. The number of applications each institution can submit is limited to two for this program because the award supports a highly non-traditional career route where investigators are able to skip post-doctoral training. The host institution supporting these individuals must be highly committed to the career development of the investigators.

One potential downside of limiting the number of applications from each institution is that factors other than science topics and the quality of the review may drive the selection process. Additionally, some members of the working group expressed concern that capping the number of applications from each institution may inadvertently introduce bias. For example, if a small amount of bias is present in a multi-step evaluation process, the bias in the end result is amplified<sup>8</sup>. However, the Early Independence Award, which does have a cap on the number of applications an institution can submit, shows drops in numbers of females throughout the review process prior to 2018, but appears to have representative numbers of females and males in the application pool. This indicates, for this award, bias may not be introduced in selecting applicants at the institution level.

Ultimately, the group decided elevating institutional diversity to a program priority could sufficiently diversify the awardee pool. Program priorities in 2018 and prior were focused on the science, potential for broad scientific impact, and scientific diversity in the HRHR portfolio.

The working group noted that if the ACD and ultimately the NIH accept this recommendation, program staff should collect data and in ten years, analyze whether the approach was successful before continuing to implement it.

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<sup>8</sup> Stephanie Johnson, David Hekman, and Elsa Chan. If there's only one woman in your candidate pool, there's statistically no chance she'll be hired (April 2016) Harvard Business Review: <https://hbr.org/2016/04/if-theres-only-one-woman-in-your-candidate-pool-theres-statistically-no-chance-shell-be-hired>

Organization	Annualized R01 \$\$/applicant	Award rate (FY2011-FY2016)				
		Pioneer	Innovator	EIA	TRA	R01s
Whitehead Institute	\$600,776.86	50.0%	0.0%	60.0%	0.0%	16.7%
Salk Institute For Biological Studies	\$368,047.10	9.1%	30.0%	100.0%	33.3%	20.7%
Gladstone Institutes	\$325,311.02	25.0%	16.7%	0.0%	0.0%	20.6%
Scripps Research Institute	\$320,865.36	10.0%	13.3%	0.0%	0.0%	15.8%
Harvard Medical School	\$313,317.46	19.0%	8.7%	37.5%	13.0%	22.8%
Rockefeller University	\$304,335.18	0.0%	41.7%	20.0%	33.3%	25.0%
Fred Hutchinson Cancer Research Center	\$295,390.48	0.0%	7.7%	16.7%	0.0%	19.7%
Massachusetts Institute of Technology	\$293,506.52	11.1%	17.1%	28.6%	22.2%	20.2%
Dana-Farber Cancer Institute	\$269,517.36	16.7%	14.3%	0.0%	15.4%	20.4%
California Institute of Technology	\$264,438.76	33.3%	50.0%	25.0%	13.3%	22.8%
Harvard T.H. Chan School of Public Health	\$259,019.62	16.7%	10.0%	0.0%	0.0%	16.6%
Stanford University	\$247,294.28	4.9%	21.2%	45.5%	8.5%	19.6%
Princeton University	\$242,104.60	30.8%	55.6%	50.0%	0.0%	23.2%
Sanford Burnham Prebys Medical Discovery Institute	\$241,301.80	0.0%	16.7%	N/A	0.0%	11.3%
Yale University	\$238,602.66	6.9%	12.7%	40.0%	2.9%	17.0%
Cold Spring Harbor Laboratory	\$235,028.66	0.0%	0.0%	50.0%	0.0%	23.5%
Memorial Sloan Kettering Cancer Center	\$234,078.38	16.7%	23.8%	0.0%	0.0%	22.5%
Harvard University	\$228,091.86	12.5%	15.8%	45.5%	8.3%	20.1%
University of Pennsylvania	\$227,666.88	3.3%	9.4%	42.9%	0.0%	18.4%
Washington University	\$226,725.42	13.3%	7.3%	20.0%	8.3%	18.7%
Boston Children's Hospital	\$224,786.90	10.0%	14.8%	0.0%	0.0%	18.2%
University of California, Berkeley	\$224,113.32	0.0%	28.9%	40.0%	0.0%	22.3%
Brigham and Women's Hospital	\$213,383.76	4.5%	5.6%	55.6%	6.9%	14.9%
Boston Medical Center	\$211,295.56	N/A	100.0%	N/A	0.0%	13.1%
Johns Hopkins University	\$210,778.82	6.1%	1.5%	18.2%	5.3%	17.8%

Lower award rate and \$/applicant  Higher award rate and \$/applicant

Figure 4. HRHR Award Rates (FY2011-FY2016) for Top 25 NIH-funded Organizations (R01 \$\$/applicant; FY2006 – FY2010). HRHR award rates were calculated based on the number of awards/number of applications and sorted by annualized R01 dollars per applicant. R01 dollars per applicant from FY2006-FY2010 were used to identify organizations with a history of NIH funding in the five years preceding the timeframe of interest for HRHR awards. Award rates for HRHR grants are shown next to award rates for R01 grants for comparison. All organizations listed received at least 1 HRHR award. N/A indicates that applications were not received in a particular category. The full table for HRHR Award Rates for 116 NIH-funded Organizations (FY2006 – FY2010) and additional data are found in the appendix.

Proposal of steps that NIH might take to enhance the diversity of investigators of institution applicants and awardees in these programs, while maintaining a focus on supporting the best science

Detailed in the section below, the working group has developed several recommendations to be considered by the Advisory Committee to the Director for ways in which to increase diversity across the applicant and award stages while ensuring that the purpose of the high risk-high reward programs is fully realized.

## RECOMMENDATIONS

### Outcomes

The working group agrees there is value in having HRHR programs and that the awards have greater influence on certain scientific areas as compared to traditional R01s. In general, they felt that the HRHR programs are successful, and recommend that NIH continue to expand them if possible.

The working group supports formal evaluation of the Transformative Research Award program through an external entity, as has been done with two other HRHR programs as described above.

### Outreach

The HRHR working group recognizes that encouraging women and underrepresented groups to serve as investigators for HRHR awards is of critical importance to increase their representation among the awardees. Specific outreach activities include:

- Initiate a special HRHR program that requires a collaboration between an under-resourced institution and resourced institution and addresses diversity in the broadest sense
- Seek specific opportunities to disseminate information about the HRHR programs to a broad audience, including at large national meetings where career sessions could feature HRHR program information
  - The working group recommends that HRHR programs should be given a speaking slot at NIH Regional seminars
- Maintain the career development portal that centralizes all NIH training grants and efforts. In addition, rather than limiting this portal to training grants, ACD should consider broadening this site to cover opportunities along the career continuum
  - <https://researchtraining.nih.gov/>
  - <https://researchtraining.nih.gov/programs/other-training-related>
- Host workshops where institutions can send 1-2 students to learn about career advancement opportunity provided through the Early Independence Award
- Offer and distribute widely outreach activities (e.g., interactive webinars) on HRHR programs
  - Distribute to current participants in NIH training award programs
  - Provide on the HRHR website prototype example grants similar to the template examples available for R01s and K awards
- Provide through program staff proactive encouragement and information, including sample applications, to prospective applicants to HRHR programs when participating on panels and other meetings
- Apply HRHR features (e.g., review mechanisms and lack of preliminary data required to apply) to other NIH grants to enhance broader success of underserved groups
  - Apply New Innovator features to a special award type for Early Stage Investigators (ESIs)

- In concert with recommendations of the Next Generation Research Initiative ACD Working Group, this group also supports expanding for Early Stage Investigators funding mechanisms that do not require preliminary data

### Bias

The HRHR working group supports efforts to encourage diversity, prevent bias, and reduce skews in research topics and institutions.

### Diversity of Applicant and Awardee Pools

Average representation of females and underrepresented minorities in the applicant pool is reflected in the awardee pool, but there is fluctuation from year to year and the numbers are small. The group agrees potential for unconscious bias should be mitigated. Potential means to address unconscious bias may include:

- Reviewer education or training, including online modules including topics such as unconscious bias
- For the Pioneer and Early Independence awards, withhold the biosketch from the first phase scientific review in an attempt to focus on the approach and more on the person in the second phase of review

### Diversity of Reviewers

- Improve and ensure racial, ethnic, and gender diversity in reviewer panel composition
  - Reviewers should also be expert in various backgrounds, as appropriate to evaluate the applications for the HRHR programs
  - Reviewers should come from a range of different institutions and organizations, from highly resourced to less well-resourced and from geographically diverse locations
- Continue to track this element and ensure representation on review panels

### Topic Bias

The group acknowledges that there appears to be bias in the topics that are awarded under HRHR programs. Clinical studies tend to be underrepresented, as do other behavioral, psychological, and sociological topics. Recommendations to address this issue include:

- Design a special track or separate HRHR program for clinical outcomes
  - Separate review track
- Reiterate in FOAs for HRHR awards that all topics are welcome and emphasize underrepresented topics
- Continue to:
  - Ensure reviewer expertise in topics underrepresented in award topic maps
  - Match reviewer expertise to applications

### Institutional Bias

HRHR awardee institutions heavily represent a subset of the top-tier research institutions. The working group recommends:

- Elevating institutional diversity as a program priority
- Evaluating the institutional diversity in 10 years to gauge the impact of this modification

### Work Environment and Harassment

The working group highlighted the importance of safe, inclusive work environments for diversity in the scientific workforce overall, including in HRHR programs. Specifically, the working group recommended:

- Requiring HRHR grantee organizations to provide assurances that they have effective, fair, and up-to-date policies to preserve a harassment-free environment
- If HRHR grantee institutions become aware of harassment findings related to HRHR grantees, they should alert and work with NIH to arbitrate the situation(s)

The working group noted and is supportive of other complementary activities that the NIH is currently undertaking, including convening a Working Group of the Advisory Committee to the Director (ACD) to focus specifically on this topic.<sup>9</sup> In September 2018, the NIH published a revised Policy Manual Chapter on Preventing and Addressing Harassment and Inappropriate Conduct, and a Federal Register Notice to share that NIH expects that organizations receiving NIH funds have in place similarly rigorous policies and related procedures for their employees, contractors, trainees, and fellows who engage in agency-funded activities.<sup>10,11</sup> In addition, the NIH Director Dr. Collins and NIH Leadership recently released a letter to university research leaders informing them of NIH's expectations of grantee behavior<sup>12</sup>.

The working group also supports the activities and recommendations of the Advisory Committee to the Director (ACD) Working Group on Changing the Culture to End Sexual Harassment.

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<sup>9</sup> <https://acd.od.nih.gov/working-groups/sexual-harassment.html>

<sup>10</sup> <https://policymanual.nih.gov/1311>

<sup>11</sup> <https://www.federalregister.gov/documents/2018/09/20/2018-20505/notice-of-new-nih-policy-manual-1311-preventing-and-addressing-harassment-and-inappropriate-conduct>

<sup>12</sup> <https://www.nih.gov/about-nih/who-we-are/nih-director/statements/update-nihs-efforts-address-sexual-harassment-science>

## APPENDIX

### Charge

The HRHR working group will review the effectiveness of distinct NIH HRHR research programs that emphasize exceptional innovation. For these HRHR programs, we will analyze the participation of women and underrepresented groups and examine institutional diversity in the applicant and awardee pools to identify possible causes for their underrepresentation. After evaluating and analyzing the HRHR programs, the working group will propose steps that NIH might take to enhance the diversity of applicants and awardees in these programs, while maintaining a focus on supporting the best science.

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### HRHR Award Rates for 116 NIH-Funded Organizations (FY2006 – FY2010)

*Appendix Figure 1. HRHR Award Rates for 116 NIH-funded Organizations (R01 dollars per applicant; FY2006 – FY2010). Organizations were sorted by annualized dollar/applicant (FY2006-FY2010) and HRHR award rates (FY2011 – FY2016) were calculated based on the number of awards/number of applications. Award rates for HRHR grants are shown next to award rates for R01 grants for comparison. All organizations listed received at least 1 HRHR award. N/A indicates that applications were not received in a particular category.*

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Percent of Total HRHR Awards for 116 NIH-Funded Organizations (FY2006 –FY2010)

*Appendix Figure 2. HRHR Award Count and percentage of total awards for 116 NIH-funded Organizations (R01 dollars per applicant; FY2006 – FY2010). Organizations were sorted by annualized R01 dollars/applicant (2006-2010). Percentage of total HRHR awards and HRHR award count (FY2011 – FY2016) are shown.*

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